

niosome structure instead of forming a stable complex. Hence, although a steroid-containing niosome and a steroid-including cyclodextrin complex have been used independently in pharmaceutical industry (see *Acta Pharma* 2005 55, 139-156; and *Drug Discovery Today: Technologies* 2005 2(1), 57-74), at the time of the present invention, no one had ever achieved a niosome composition for enhanced transdermal delivery of steroid compounds (as recited in pending claim 1).

In order to reject claims as being obvious over a combination of prior art references, there must be a reasonable expectation of success. See M.P.E.P. 2143.02, citing In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) and Ex parte Blanc, 13 USPQ2d 1383 (Bd. Pat. App. & Inter. 1989). Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart, 189 USPQ 143 (CCPA 1976). Whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. Ex parte Erlich, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986).

In the present case, the pending claims were rejected based on a combination of Vyas et al. (disclosing niosomes including steroids and non-ionic surfactants) and Pitha (disclosing an inclusion complex between a steroid and a cyclodextrin compound). The Examiner contended that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising a niosome comprising the cyclodextrin derivatives and the surfactants as instantly claimed since the niosomes containing steroidal active agents analogous to the instant niosomes are seen to be taught in the prior art." The motivation for this combination was explained to be "since niosomes containing drugs are able to penetrate the stratum corneum and appears promising for the transdermal delivery of even hydrophobic and amphiphilic drugs (Vyas, page 63, section 8.7 through page 64). Using complexes of cyclodextrin with the steroidal drugs would ensure more of the active agent being transported across the skin due to increased solubility." However, the evidence submitted with this response indicates that a person of ordinary skill in the

art, at the time the invention was made, would not have had a reasonable expectation of success in achieving a niosome composition containing a steroid and a cyclodextrin compound, as claimed. At the time of the invention, those skilled in the art believed that adding a cyclodextrin compound to a steroid-containing niosome resulting in removal of the steroid compound from the lipid bi-layer of the niosome, resulting in disruption of the niosome structure. The presently pending claims therefore cannot be rejected under 35 U.S.C. 103(a) as being obvious, as the evidence provided shows that a person of ordinary skill in the art at the time of the invention would not have had a reasonable expectation of success in combining the prior art references of record in the manner claimed.

The present invention was made to overcome the failure of others, by first forming a steroidal agent containing cyclodextrin inclusion complex, followed by mixing the inclusion complex with a niosome formed by non-ionic surfactant. A composition thus formed does not have the drawbacks of the prior composition, that is, extraction of steroid compounds from the niosomes due to the addition of cyclodextrin. Furthermore, the composition thus formed (*e.g.*, the composition of instant claim 1) exhibits enhanced transdermal delivery of steroid compounds as compared with that of the known niosomes (See Example 7 of this instant invention). Therefore, the composition of instant claim 1 is both novel and nonobvious in view of the combined teaching of the cited references.

In view of the above, it is respectfully submitted that claims 1-6, 8-14 and 16-19 are patentable over Vyas *et al* (International Journal of Pharmaceutics. 1998, 172, 33-70) in view of Pitha (US 4,727,064). The Examiner is accordingly respectfully requested to pass this application to allowance.

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-4-

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